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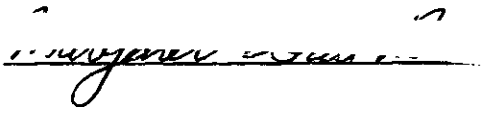

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THE EFFECTS OF AMOBARBITAL ON STIMULUS CONTROL

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SUMMARY

For many behaviorally active drugs, including amobarbital, the function relating the drug rate of responding to the control rate of responding is inverse. That is, low control rates of responding are increased under the drug while high control rates are decreased. This inverse relationship between drug rates and control rates is referred to as the drug rate-dependency effect.

Drug rate-dependency effects may be modified by the use of powerful stimulus events or by the use of procedures for establishing strong stimulus control. Such "stimulus-dependent" effects suggest the possibility of using drugs as tools to study the extent of control that a particular stimulus exerts on behavior.

The present study was conducted to determine if there was a difference in the amount of stimulus control exerted by three different stimulus procedures used to produce a near-zero level of responding. These three procedures were: (1) S^{Δ} (a stimulus in whose presence reinforcement is never delivered); (2) S^{Δ}'s which were terminated with the presentation of a brief electric shock; and (3) S^{Δ}'s which were terminated with the presentation of a brief stimulus (S^{P}) which always accompanied food. Rats were used in

procedures 1 and 2 and pigeons were used in procedures 1 and 3. The S^{Δ}'s in each of these three procedures were superimposed on the odd-numbered minutes of a fixed-interval ten-minute schedule.

Although all three stimulus procedures controlled a near-zero level of responding, the effects of amobarbital varied. Rate-dependency functions were obtained under the simple S^{Δ} procedure for both the rats and pigeons. When a brief shock was added to the S^{Δ}, results varied depending on the amperage level used. At low amperage levels (0.13 and 0.25 ma) rate-dependency functions were still obtained while at high amperage levels (0.50 and 0.80 ma) the rate-dependency effect was abolished. When a brief S^{P} was added to the S^{Δ}, there was no change in the rate-dependency functions obtained.

These results indicate that there were no differences in the amount of stimulus control exerted by the S^{Δ} or the S^{Δ} plus S^{P} stimuli for the pigeons. However, for the rats, the amount of stimulus control exerted by the S^{Δ} plus shock was much greater than that held by the simple S^{Δ} procedure, especially when high amperage levels were used. Amobarbital was thus useful as a pharmacological tool for detecting differences in the degree of stimulus control exerted by three stimulus procedures which produced very similar baseline performances.

CHAPTER I

LITERATURE REVIEW

Introduction

Most of the research that has been directed toward discovering the behavioral effects of drugs has been done since 1950. The increased interest in behavioral research at this time was due partly to the synthesis of chlorpromazine (CPZ) in 1950 (Caldwell, 1970). Chlorpromazine was specifically synthesized to be used as a preparation for surgical patients. Its purpose was to alleviate anxiety and stress in pre-operative patients and to facilitate recovery after surgery.

Shortly after chlorpromazine was found to be an effective anti-anxiety agent in surgical patients, it came to the attention of psychiatrists who wanted effective drugs which could be used for the treatment of depression, clinical anxiety, schizophrenia and other behavioral disorders. The use of chlorpromazine stimulated the synthesis of new drugs as well as the rediscovery of many older drugs such as meprobamate, imipramine, promazine and reserpine, which had not previously been used in the therapy of major mental illness. The emphasis at this time was directed toward the effects of drugs on emotional behavior and the drugs of

interest were designated "stimulants", "tranquilizers" and "anti-depressants".

One approach to the study of the effects of behaviorally active drugs involved the development of situations using infrahuman subjects in which the animals' behavior would resemble a particular human behavior which was of concern. This approach, in effect, attempted to establish animal models of human behavior disorders so that the effects of drugs upon these disorders could be studied. It was thought that if there existed a reliable method for producing a behavior similar to clinical anxiety, for example, more could be learned about the conditions under which tranquilizers or other drugs might affect this behavior. Such an approach might also aid in the discovery of new effective agents.

One animal model described the occurrence of "experimental neurosis" in dogs when they were forced to make discriminations between two nearly identical stimuli. Such dogs may whine, struggle when restrained, refuse to eat and appear to be "nervous". This general procedure was an appealing tool for investigating emotional behavior since it resembled, in some ways, the behavior seen in neurotic humans. Masserman (1959) studied the effects of several drugs on this model extensively and reported that some agents such as chlorpromazine, alcohol, and meprobamate,

appeared to attenuate the neurotic behavior. However, the "experimental neurosis" proved to be a very complex behavior, and no agreement as to the necessary and sufficient conditions required to produce it was reached (Harvey, 1971).

Several other procedures involved the conditioning of a particular response in the animal and then measuring the extent to which the conditioned response failed to occur following the administration of a particular drug. Many experimental procedures involved the use of a noxious electric shock. In some of these procedures, the responses that were conditioned were usually described as "fear", "anxiety" or "conditioned emotional" responses and were thought by some to contain elements which were analogous to clinical anxiety on the human level.

One of the most frequently used "anxiety" responses was the pole climbing response used by Couvoiser et al. (1953). This procedure involved sounding a buzzer at which time a rat had to scale a pole in order to avoid an electric shock. A similar response was used by Jacobsen (1957) and Bättig (1957). This response was barrier crossing, which involved the animal moving from one part of a cage to the other at the onset of a signal in order to avoid an electric shock. Several studies which used such conditioned avoidance responses (CARs) are discussed by Dews and Morse (1961), Cook and Kelleher (1963) and Cook and Catania (1964).

Other more elaborate procedures for studying drug effects involved the use of schedule-controlled behaviors. Schedule-controlled behavior is established using operant conditioning techniques. A schedule specifies the relationship between environmental stimuli, a given response of the animal, such as the pecking response of the pigeon or a bar-press response in the rat, and the presentation of an event, e.g., a reinforcer, such as food, water or removal of a noxious stimulus. There are two basic types of schedules relating the occurrence of a response to the presentation of a reinforcer (Ferster and Skinner, 1957). The interval schedule specifies that a response will be reinforced on the basis of time. The ratio schedule specifies that reinforcement will be delivered on the basis of the number of responses that have occurred. Under fixed-interval (FI) schedules, the reinforcer follows the first response that occurs after a constant interval of time has elapsed from some specified event. Thus, with a fixed-interval five-minute schedule the first response to occur after five minutes has elapsed from some specified event will be reinforced. Under variable interval (VI) schedules, the amount of time that must elapse will vary from one reinforcement to the next. The mean time requirement is specified. Under a fixed-ratio (FR) schedule, reinforcement is presented after a constant number of responses have been emitted.

Thus under a fixed-ratio fifty schedule, reinforcement is presented after fifty responses have been made. Under a variable-ratio (VR) schedule the number of responses required vary from one reinforcement to the next around some mean value.

These schedules of reinforcement engender reproducible temporal patterns of responding which can be objectively measured. In general, a particular pattern of responding is characteristically produced by a specific reinforcement schedule.

Patterns of responding are typically recorded on a cumulative recorder. A roll of paper moves slowly around a cylinder. Each response made by the animal moves an ink pen one small constant increment upward on the vertical axis of the paper. Thus, if the animal never responded, a straight, horizontal line would be produced. As an animal responds more frequently, a curve or a line with greater slope is produced. Such a continuous record of the organism's responding is exceedingly useful in the study of drugs since the time course of action of the drug effect on behavior can be readily observed.

Conditioned Suppression

One of the earliest animal models which used schedule-controlled behavior to study drug effects was the conditioned suppression procedure developed by Estes and Skinner (1941).

The conditioned suppression procedure utilized a fixed-interval five-minute schedule for food reinforcement. Rats were used as subjects. Under a fixed-interval schedule, an initial period of no responding is followed by acceleration of responding to a final rate that is sustained until reinforcement is delivered. This pattern is frequently referred to as a scallop. After a few sessions, Estes and Skinner superimposed a tone stimulus which terminated with shock on the food-maintained baseline of responding. Both the presentation of the tone and the shock were independent of the subject's responses. After a few tone-shock trials, the food-maintained responding became totally suppressed during the presentation of the tone (the pre-shock stimulus). Responding resumed immediately, however, as soon as the tone, and the coincident shock terminated. The shape of the fixed-interval cumulative response curve was thus not affected except during the tone presentation.

Estes and Skinner concluded that the suppression effect was due to the Pavlovian conditioning of "anxiety" during the tone. Certain autonomic responses (such as increased heart rate, respiration, etc.) as well as skeletal muscle responses (freezing, crouching, etc.) came to be elicited by the pre-shock stimulus. These conditioned anxiety responses supposedly competed with the food-maintained responses so that suppression was observed.

The conditioned suppression paradigm also had appealing face validity as an animal analog of human psychiatric disorder. Motivational interpretations of drug effects held that good "tranquilizing" drugs would alleviate internal anxiety states so that "anxiety" responses would no longer interfere with other responses such as food-maintained responding in animal experiments. Consequently, the effects of a large number of behaviorally active drugs have been studied on conditioned suppression. Among these drugs are reserpine (Brady, 1956; Weiskrantz and Wilson, 1956; Sidman, 1956; Ray, 1964; Unemoto, 1962; Kinnard, Aceto and Buckley, 1962; and Valenstein, 1959), amphetamine (Brady, 1956; Lauener, 1963), morphine (Hill, Pescor, Belleville and Wikler, 1957; and Lauener, 1963), chlorpromazine (Hunt, 1957; Lauener, 1963; and Ray, 1964), the barbiturates phenobarbital, barbital, aprobarbital and amobarbital (Lauener, 1963) and chlordiazepoxide (Lauener, 1963).

The effects of reserpine on conditioned suppression have been most extensively studied. Brady (1956), Weiskrantz and Wilson (1956), Sidman (1956) and Ray (1964) found that reserpine reinstated responding which had been suppressed during the presentation of the pre-shock stimulus. However, other investigators (Unemoto, 1962; Kinnard, Aceto and Buckley, 1962; Stein, 1956 and Valenstein, 1959) found that reserpine had little effect on the suppressed responding.

Similar results were reported for the barbiturates. The lack of generality in the results using conditioned suppression have disappointed investigators who assumed both that suppressed responding in the presence of a pre-shock stimulus is an animal analogue of anxiety and that tranquilizing drugs have specific effects on anxiety.

The different findings which have resulted using conditioned suppression are difficult to evaluate due to the use of different schedules, shock intensities and parameter values. Several reviews discuss variables which influence conditioned suppression (Kelleher and Morse, 1968; Davis, 1968 and Church, 1969) and which may, as a consequence, influence the effects of drugs on suppressed behavior. One variable which is particularly important is punishment. It has been suggested that the rate of responding may be decreased to a very low level in the presence of the pre-shock stimulus due to adventitious punishment. Azrin (1956) compared the conditioned suppression procedure with a similar procedure in which a response produces an immediate shock. Azrin found that although suppression was much greater when responses immediately preceded shock, suppression also occurred when shocks followed responses after specified delays.

The results of several studies have important implications for determining the extent to which adventitious

punishment may be involved in producing the suppression effect (Geller and Seifter, 1960, 1962; Geller et al, 1962; Morse, 1964; Kelleher and Morse, 1964). These studies have shown that certain drugs consistently increase responding that has been suppressed by immediate punishment. Among these drugs are pentobarbital, amobarbital, phenobarbital, meprobamate and chlordiazepoxide. These drugs are thought to affect punishment specifically since drugs such as chlorpromazine, which is considered to be a powerful tranquilizing agent, do not increase responding which has been suppressed by punishment. These findings suggest the possibility that drugs may be used as tools to uncover different behavioral processes that may be active in a particular situation. This possibility would rest on the demonstration that particular drugs have specific, rather than general effects, on a particular behavioral process. If it can be reliably demonstrated that minor tranquilizers have a specific effect upon responding suppressed by punishment, the effect of these drugs upon conditioned suppression may provide information as to the role that adventitious punishment may play in producing the suppression effect.

Another recent finding which has challenged the interpretation that the conditioned suppression phenomenon is due to the Pavlovian conditioning of an anxiety response is the discovery that responding can also be suppressed in

the presence of a stimulus terminated by a response-independent reinforcer. Such suppression of responding is referred to as positive conditioned suppression. Azrin and Hake (1969) demonstrated response suppression when food, water or brain stimulation was used instead of an electric shock. In this study rats were trained to press a lever on a variable-interval schedule to obtain food or water reinforcement. After a stable rate of responding was obtained, they superimposed either a red flashing light or a buzzer which terminated with either free food, free water or brain stimulation. This resulted in the suppression of responding during the "pre-reinforcement" stimuli. Azrin and Hake suggested that the effect might be due to a conditioned "elation" response. The finding that suppression may be produced without the presentation of a noxious stimulus severely questioned the use of this procedure as an "anxiety" model.

An alternative to motivational interpretations of drug effects is to study the effects of the drug upon particular characteristics of the behavior. Using this approach, behavior is described in terms of the pattern and rates of responding that develop when different schedule contingencies are in effect. The effects of drugs on these rates and patterns of responding reveal interesting and consistent results.

Drug Rate-Dependency

One of the first important observations relating drug behavior to nondrug behavior was made by Dews (1958a). Dews studied the effect of pentobarbital on a multiple fixed-ratio 50 fixed-interval 5-min schedule in the pigeon. When a red keylight was presented, the fixed-ratio 50 was in effect. That is, every fiftieth peck on the key was reinforced. Consequently, a high, steady rate of responding developed during the red stimulus. When the keylight was blue, however, a fixed-interval 5-min schedule was in effect. The typical fixed-interval pattern of accelerated responding developed during the blue stimulus. When pentobarbital was administered, Dews observed that while the fixed-ratio responding was not at all disturbed by the drug, responding in the fixed-interval component was greatly disrupted. However, the difference in the control rate of responding under the two schedules was also notably different before the drug was ever administered. Dews observed that one of the basic differences between these two schedules was in control rate of responding. Dews suggested, therefore, that the control rate of responding might influence the drug rate of responding. The fixed-ratio schedule produced high control rates and because of this, Dews suggested that the fixed-ratio schedule maintained more stimulus control over responding. This is consistent with Dews'

(1955) study which showed that the fixed-ratio performance was less disrupted by pentobarbital than the fixed-interval performance. These results are also consistent with those of Herrnstein and Morse (1956) who found that pentobarbital acted to fractionate fixed-interval fixed-ratio performance by selectively eliminating the fixed-interval behavior and leaving the fixed-ratio component of the schedule untouched.

In a subsequent study, Dews (1958b) investigated more extensively the role of control rate of responding in determining the drug rate of responding. Dews studied the effects of methamphetamine on four schedules of food reinforcement in the pigeon. Two schedules, a variable-interval 1-min and a fixed-ratio 50, generated high rates of responding. Low doses had little effect on response rate on either schedule, but higher doses decreased the rate of responding on both. The other two schedules, a fixed-interval 15-min and a fixed-ratio 900, generated low rates of responding. Low doses of methamphetamine greatly increased the response rate under these two schedules. Higher doses decreased the response rate. Methamphetamine affected responding by reducing the high control rates characteristic of the first two schedules and increasing the low control rates engendered by the latter two schedules. This inverse relationship, low control rates are increased while high control rates are decreased, is referred to as the drug

rate-dependency effect. Thus control rate can be an important determinant of the behavioral effects of drugs.

Rate-dependency has been demonstrated for behavior maintained by both positive and negative reinforcers. Waller and Waller (1962), using Beagle dogs as subjects, studied the effects of chlorpromazine on a complex schedule having two basic components. One component was a variable-interval 1-min schedule during which the dogs responded for food reinforcement. The other component was a Sidman avoidance schedule during which the subjects responded in order to avoid shock. During the avoidance component, a shock was delivered every 20 seconds unless the subject responded. If the subject responded, the shock was delayed for 20 seconds from the time of the response. When output ratios (i.e., the mean drug rate divided by the mean control rate plotted as a function of dosage) were computed, there was little difference between the effects of chlorpromazine on the food-maintained behavior and the avoidance maintained behavior over a considerable range of doses.

McMillan (1971) studied the influence of the schedule of reinforcement on the rate-dependency function. McMillan used a multiple fixed-interval fixed-ratio schedule; however, the parameters of the two schedules were manipulated so that similar control rates were produced by both schedules. This was done by increasing the fixed-interval rates and decreasing

the fixed-ratio rates. The fixed-interval rates were increased by using a short interval (FI 1-min). The fixed-ratio rates were decreased by increasing the response requirement to 150. Thus the final schedule was a fixed-ratio 150 fixed-interval 1-min schedule. McMillan found that under these conditions the effects of amphetamines were determined more by the control rate of responding than by the particular schedule generating the responding. Thus, the schedule is an important determinant of the effects of a drug on behavior since the schedule influences the control rates of responding that are obtained.

That certain stimulus situations should influence the effects of drugs on behavior should not be surprising since various aspects of stimulus control influence the rate of nondrug responding. When food is presented under an intermittent schedule in the presence of one stimulus (S^D) but never in the presence of another stimulus (S^Δ), these stimuli come to exert differential control over the rate of responding. In operant conditioning, discriminative stimuli (S^D) are said to control the operant response. These stimuli control behavior in the sense that responses occur at a high rate in the presence of a stimulus that has accompanied the occurrence of the response in the past and has set the occasion for its reinforcement. S^Δ stimuli typically command low rates of responding, since their

presentation is associated with non-reinforcement. In this instance, stimulus control is demonstrated by the fact that the organism consistently responds in the presence of one stimulus and does not respond in the presence of another stimulus.

Several studies have investigated the effects of superimposing S^{Δ} periods on schedules of reinforcement (Ferster and Skinner, 1957; Dews, 1964, 1965a, 1965b; Farmer and Schoenfeld, 1966; and Lyon and Miller, 1969). In Dew's study (1964) a multiple S^{Δ} procedure was developed. Pigeons were first trained to peck under a fixed-interval 500-sec schedule. When a stable baseline had developed, the 500-sec interval was divided into ten segments of 50-sec each during which S^{Δ}'s were superimposed. The houselight (HL) which served as the S^{Δ} was on during the 1st, 3rd, 5th, 7th and 9th segments. During the 2nd, 4th, 6th, 8th and 10th segments the houselight was off. Thus a response was reinforced only in the absence of the houselight. As a result of these stimulus conditions, responding dropped to an almost zero level in the odd-numbered segments, but during the even-numbered segments, response rates were almost identical to the rates in the corresponding segments of the baseline fixed-interval. The shape of the fixed-interval was, therefore, not appreciably altered.

When amobarbital was administered, low control rates were increased while high rates either remained the same or

were slightly decreased. That is, a drug rate-dependency effect was demonstrated. Dews quantified this rate-dependency relationship in the following manner: if the drug rates in each segment of the fixed-interval are divided by the corresponding control rates, the resulting ratios express the relative changes in rate that the drug induces. If these ratios are then plotted against the control rates on logarithmic coordinates, the resulting function is a straight line with negative slope. Such a regression line has subsequently been found to characterize many rate-dependency effects.

Dews' study, however, revealed another interesting finding. Even though the control rates of responding in the S^{Δ} segments were lower than the comparable control rates under a regular fixed-interval schedule, all the data points fell on the same regression line. That is, there was a much greater proportionate increase in the rates of responding in the S^{Δ} segments than in the comparable segments under the regular fixed-interval. Thus the fact that the houselight acted as an "inhibitory" stimulus commanding low control rates did not alter the rate-dependency function. This finding led Dews to conclude that the sole determinant of the effect of amobarbital was the control rate of responding. The particular stimulus procedures used to produce low rates did not alter the

rate-dependency relationship.

Modifications of Drug Rate-Dependency

There is now increasing evidence that certain stimulus events and procedures for establishing stimulus control may modify the rate-dependency effects that a drug has on behavior. McKearney (1970), for example, has found that rate-dependency functions obtained using amobarbital could be modified by varying stimulus control procedures. McKearney also used a fixed-interval 10-min schedule with superimposed $S^{\triangle}$s. However, two different methods of presenting the $S^{\triangle}$ stimuli were used. Under the first procedure, a red keylight was presented during the even-numbered (S^{D}) minutes. During the odd-numbered ($S^{\triangle}$) minutes, the keylight remained red, but every response produced a 3-sec change of the keylight color to green. Under the second procedure, referred to as the continuous keylight procedure, a red keylight was again continuously presented during the even-numbered minutes, but during the odd-numbered minutes, the keylight was continuously green.

When amobarbital was administered, it was found that the rate-dependency effect was again demonstrated but the rate-dependency function for the $S^{\triangle}$ points was different from the rate-dependency function for the S^{D} points. That is, the two different regression lines indicated that the

increases in the S^{Δ} responding were much less than would be expected if the magnitude of the increase depended solely upon the control rate of responding. If the sole determinant of a drug behavior was the control rate, then all the data points (S^{D} as well as S^{Δ}) would have fallen along the same regression line, the results reported by Dews. When McKearney replicated this study using a houselight as Dews did, he found that all the data points fell on the same line. When the intensity of the houselight was varied, however, the results also varied. It was found that when a relatively dim (500 or 700 ohm resistence in series) houselight was used for the S^{Δ}'s, all the data points fell above the S^{D} regression line, even though the control rates for both dim and bright houselights were the same.

McKearney concluded that the bright houselight as well as the keylight maintained more stimulus control over responding than did the dim houselight and as a consequence the rate-dependency effect of amobarbital was modified. This interpretation is consistent with the results obtained by Weiss and Laties (1966) which showed that the effects of drugs on a fixed-interval schedule were lessened considerably when a "clock" was added: that is, a different stimulus was associated with each minute of the (5-min) interval. Under these conditions the stimulus in the last minute, which is present when food is presented, functions as an S^{D}. All the other stimuli are equivalent to S^{Δ} stimuli. Giving the birds

a "clock" greatly decreased the effects of amphetamine, scopolamine and pentobarbital.

Laties and Weiss (1966) observed that the baseline rates were relatively unimportant in determining the drug effects when the "clock" was added and thus concluded that the control rates were relatively unimportant in predicting drug effects when the behavior is controlled by powerful discriminative stimuli.

Terrace (1963) also found varying drug effects for pigeons who learned discriminations with and without errors. In the errorless discrimination learning procedure, the pigeons were trained to discriminate between two stimuli, S+ (S^D, a red keylight) and S- (S^Δ, a green keylight) with no errors; i.e., with no responses ever being made in the presence of S-. Terrace found that the effects of chlorpromazine and imipramine on discrimination performance were different for the two groups of birds. Neither imipramine nor chlorpromazine had any effect on responding to S- for birds who received discrimination learning without errors but that both drugs greatly increased responding to S- for those birds who learned the discrimination with errors.

Terrace concluded that the S- assumed aversive properties for the birds who learned the discrimination with errors due to responding in the presence of the non-reinforced stimulus during training. Chlorpromazine and imipramine increased responding to the S- by reducing the

aversiveness of the S-. The alternative explanation is that discriminations which are learned without errors acquire more stimulus control over behavior than discriminations which are learned with errors.

Modification of rate-dependency by using different stimulus events and different methods of presenting stimuli has become the focus of an increasing number of studies. Holz (1971) studied the effects of chlorpromazine on conditional discriminations. Conditional discriminations require two items of information in combination to determine a correct response. For example, if a comparison light is red, a pigeon must peck the red key, but if the comparison light is blue, then the pigeon must peck the blue key. In discriminations involving oddity, the pigeon would have to peck the key that was different in color from the comparison light.

Chlorpromazine typically reduces the accuracy of pigeons on conditional discriminations. Holz demonstrated that the pigeons' reduced accuracy on these discriminations is a function of the drug's rate-dependent effects. That is, chlorpromazine reduces the pigeon's accuracy by decreasing the number of correct responses (which normally occur at a high rate) and increasing the number of error responses (which normally occur at a low rate). Holz also noted that when the regression analysis was performed, the

intercept of the regression line for the error responding was lower than the comparable intercept for correct responding. That is, two different functions were needed to describe the effect of chlorpromazine on rate of responding, one for error responding and one for correct responding. This finding demonstrated that responses controlled by different factors, even though the control rates were the same, may be affected differently by a drug.

In another study, McMillan (1971) found that the drug rate-dependency function could be modified by the response-produced presentation of electric shock (punished responding). McMillan studied the effects of d-amphetamine on a multiple FI FI schedule where each response during one of the FI components produced an electric shock. Contrary to the finding of Geller et al. (1960), McMillan found that the rate-dependent effect of d-amphetamine held for punished as well as for the nonpunished responding. There was a difference, however, between the rate-dependency function obtained from punished versus nonpunished data. The rates of nonpunished responding were increased much more than matched rates of punished responding when d-amphetamine was administered. Consequently, the intercept of the regression line was higher for the nonpunished than for the punished responding. This punishment data adds support to the notion that drug rate-dependent effects may be modified

by certain stimulus events.

The influence of stimulus control on drug rate-dependency functions becomes particularly important when very low or near zero levels of responding are engendered by the use of different stimulus procedures. When two different stimulus procedures both produce a near-zero level of responding, there often may not be any detectible differences in the baseline performance engendered by these procedures. Thus, it may be extremely difficult, if not impossible, to determine the relative amount of stimulus control that each holds over behavior. However, the amount of stimulus control may be inferred by administering a drug, such as amobarbital, and determining the extent to which the rate-dependency effect is demonstrated or the extent to which the rate-dependency function may be modified or even abolished by the use of a particular stimulus procedure.

The present study was conducted to determine by a behavioral pharmacological analysis if a difference exists in the amount of stimulus control exerted by three different stimulus procedures used to produce low levels of responding. These three procedures were: (1) S^{Δ}; (2) S^{Δ}'s which terminated with the presentation of a brief electric shock; and, (3) S^{Δ}'s which were terminated with the presentation of a brief stimulus paired with food. Rats were used in procedures 1 and 2 and pigeons were used for procedures 1 and 3.

The basic S^{Δ} procedure used in this experiment is similar to that developed by Dews (1964) and subsequently used by McKearney (1970) in illustrating the influence of stimulus control on rate-dependency functions.

Procedure 2 in which the S^{Δ}'s were terminated with the presentation of a brief electric shock is similar to the conditioned suppression procedure in that a stimulus which terminates with a brief shock is superimposed on a baseline of food-maintained responding. The primary difference between the S^{Δ} procedure with added shock and the conditioned suppression procedure is that the conditioned suppression procedure has S^{Δ} properties only when the added stimulus is superimposed on a fixed-interval baseline. When the added stimulus is superimposed on a variable-interval baseline, as has generally been the case in most conditioned suppression studies, reinforcement is possible during the presentation of the pre-shock stimulus. Since reinforcement may occur, it is difficult to determine what role shock <u>per se</u> plays as a stimulus condition. Procedure 2 of the present study permits the role of shock as an added stimulus to be studied. The basic question asked is: Does an S^{Δ} stimulus which terminates with shock maintain more stimulus control over responding than does a simple S^{Δ} stimulus? If the S^{Δ} with shock is a more "powerful" stimulus than a simple S^{Δ}, it is expected that the S^{Δ} points would be considerably below the

S^D points; that is, two regression lines (one for S^D and one for S^Δ points) would be needed to best fit the data.

The third procedure in which the multiple S^Δ's are terminated with the presentation of a brief conditioned reinforcer is similar to positive conditioned suppression. Here again, however, the positive conditioned suppression studies have also typically utilized variable-interval schedules to maintain a baseline of responding. The effects of the presentation of a positive stimulus can be studied through the use of a fixed-interval schedule without the confounding variable of having the animal receive response dependent reinforcement in the presence of the pre-reinforcement stimulus. The basic question asked here is: Does the addition of a positive reinforcer to an S^Δ stimulus change the amount of stimulus control exerted by that S^Δ?

In summary, this experiment examines the difference in stimulus control that these three methods of suppression exert over an organism's behavior. More specifically it permits a determination of the contribution that electric shock and the presentation of a positive conditioned reinforcer make in producing low rates of responding. It is increasingly important to know the relative contribution of stimulus control in determining drug effects. Since there is much interest in the effects of drugs on suppressed behavior, it is particularly important to determine to what

extent the particular method of suppressing behavior may contribute to the final effect the drug has on the behavior.

CHAPTER II

METHOD

Subjects

Five Sprague-Dawley rats designated B-2, B-3, B-6, B-7 and B-8 and four White Carneaux pigeons designated 354, 237F, 110 and 276 served as subjects. Each subject was maintained at eighty percent of its free-feeding weight. At all times in their home cages, rats had access to water and pigeons had access to grit and water. The rats were experimentally naive. Two of the rats, B-2 and B-3, were 90 days old at the beginning of the experiment. The other three rats, B-6, B-7 and B-8 were 150 days old. Prior to this experiment all birds had been conditioned to peck a transilluminated response key (Ferster and Skinner, 1957) and had performed under various schedules of food presentation.

Apparatus

The rat experiment was carried out in a standard operant-conditioning chamber, housed in a ventilated, sound-attenuating enclosure. The chamber contained a single response key that could be transilluminated by a white 6-w lamp. Three black horizontal bars on a white background or a solid black circle on a white background could be projected onto the response key. The rat was required to nose the key with

a minimum force of 0.20N in order to operate it. The grid floor was wired to a Grason-Stadler model E106GS shock generator. Reinforcement consisted of 10-sec access to liquid monkey diet. During the last three months of the experiment, reinforcement consisted of 10-sec access to either chocolate or vanilla flavored Sego.

The pigeon experiment was carried out in a similar chamber. The chamber contained a single response key that could be transilluminated by a red or green 6-w lamp. A houselight (HL) which could be transilluminated with a 12-w white light was located in the upper right-hand corner of the chamber. The response key required a minimum force of 0.20 N to operate. Reinforcement was 6-sec access to mixed grain.

Both the rat and the pigeon experiments were scheduled by relay switching circuitry and the data were recorded by impulse counters, running elapsed time meters and a cumulative recorder.

Procedure

The rats were first magazine trained and then shaped by successive approximations to nose the response key. Magazine training was not necessary for the birds since all had performed previously on schedules of reinforcement. The basic schedule for all subjects was a fixed-interval ten minute schedule. Thus the first response to occur after

ten minutes was followed by food presentation. A 30-sec timeout period, during which all lights were extinguished and responding had no scheduled consequences, followed each food presentation. The rat experiment had a 90-sec limited-hold. If no response was made within 90-sec of the end of ten minutes, the timeout was presented automatically and food was not available until the end of the next fixed-interval. Daily sessions terminated after 12 presentations of the timeout for the rats and after 14 presentations of grain for the pigeons. The stimulus conditions for the fixed-interval 10-min schedule were as follows: for the rats, a solid black circle on a white background was projected onto the response key throughout the 10-min period until reinforcement was presented. For the pigeons the response key was transilluminated with a red light throughout the 10-min period and until reinforcement was presented. During the presentation of the reinforcement, the keylight was extinguished and the magazine light was presented. White masking noise was present at all times for both the pigeon and rat experiments.

After a stable FI 10-min baseline was established, all subjects were injected twice, at two different times, with physiological saline ten minutes before the beginning of a daily session. Saline injections did not affect baseline responding. The subjects were then drugged approximately

twice a week with sodium amobarbital. The sodium amobarbital was kindly supplied by Abbott Laboratories. Injections were made approximately ten minutes before the beginning of a daily session. Each drug session was preceded by a normally executed control session the day before. The sodium amobarbital was dissolved in physiological saline. Rat injections were given intraperitoneally (IP) and pigeon injections were given intramuscularly (IM). Doses used were 10, 17 and 30 mg/kg of body weight. The doses were administered in ascending order at least three separate times for each subject.

When all data had been collected from the regular FI 10-min schedule, S^{Δ}'s were superimposed on the odd-numbered minutes (minutes 1,3,5,7 and 9) of the 10-min fixed-interval for all subjects. This condition is referred to as the FI 10-min plus S^{Δ} condition. Stimulus conditions during the even-numbered minutes (minutes 2,4,6,8 and 10), which functioned as S^{D}'s, remained exactly the same as they had been under the simple FI schedule. For the pigeons, the S^{Δ} was a green keylight. For the rats, the S^{Δ} was initially three black horizontal bars projected onto the response key. However, since the rate of responding of the rats failed to become suppressed (i.e., to approach zero) in the presence of the black bars within 14 sessions, another S^{Δ} stimulus was added. This stimulus was the absence of white noise.

Under these conditions, responding during the odd-numbered minutes fell to a low rate within two daily sessions. Thus, while the rats actually had a compound S^{Δ} stimulus, three black horizontal bars projected onto the response key and the absence of white noise, it was actually only the absence of white noise that controlled S^{Δ} responding.

When responding under the FI 10-min plus S^{Δ} condition stabilized (i.e., when the rate of responding in the presence of the S^{Δ}'s approached zero), all subjects were again drugged approximately twice a week with amobarbital using the procedure previously described. Doses in this instance, however, were administered in ascending order six (rather than three) separate times for each subject.

During the last phase of experimentation, the S^{Δ}'s for the rat experiment terminated with the presentation of a brief electric shock. This condition is referred to as an FI 10-min plus S^{Δ} plus shock condition. The duration of the electric shock was 0.5 sec. The voltage remained constant at 100-v, but four different amperage levels were used: 0.13 ma, 0.25 ma, 0.50 ma, and 0.80 ma.

During this phase of experimentation, the S^{Δ}'s for the pigeons terminated with the brief presentation of a stimulus which was also present when reinforcement was delivered. This stimulus is designated S^{P} for "stimulus paired with reinforcement". This condition is referred to

as the FI 10-min plus S^{Δ} plus S^{P} condition. The S^{P} was a 0.10 sec presentation of the houselight. The houselight was also present during the 6-sec reinforcement period.

When responding had stabilized under the FI 10-min plus S^{Δ} plus shock condition for the rats and under the FI 10-min plus S^{Δ} plus S^{P} for the pigeons, all subjects were again drugged using the previously described procedure. The pigeons were drugged eight times at each dose level. The rats, however, were drugged twice with 10 mg/kg at each amperage and twice with 17 mg/kg.

CHAPTER III

RESULTS

FI 10-Min Schedule

For both rats and pigeons performance on the FI 10-min schedule stabilized within sixty sessions. At this time no systematic changes were observed in the cumulative records, overall rates of responding, or measures of curvature for the fixed-interval pattern of responding. The dose response curve (mean rate of responding plotted as a function of dosage) for the rats for doses of 10, 17 and 30 mg/kg of amobarbital are presented in Figure 1. The overall control rate is the mean rate of responding for 35 normally executed sessions (6-8 for each of the five rats). Overall drug rates were computed from 12 drug sessions at each dose level. It may be observed from Figure 1 that the overall rate of responding progressively increased at the 10 and 17 mg/kg doses and then decreased somewhat at the 30 mg/kg dose. The dose response curve for the pigeons for doses of 10, 17, 30 and 56 mg/kg is presented in Figure 2. The overall control rate for the pigeons is the mean of 24 normally executed sessions (six control sessions for each individual pigeon). Overall drug rates were computed from eight drug sessions at each dose (two drug sessions for each individual pigeon). Overall rates of responding

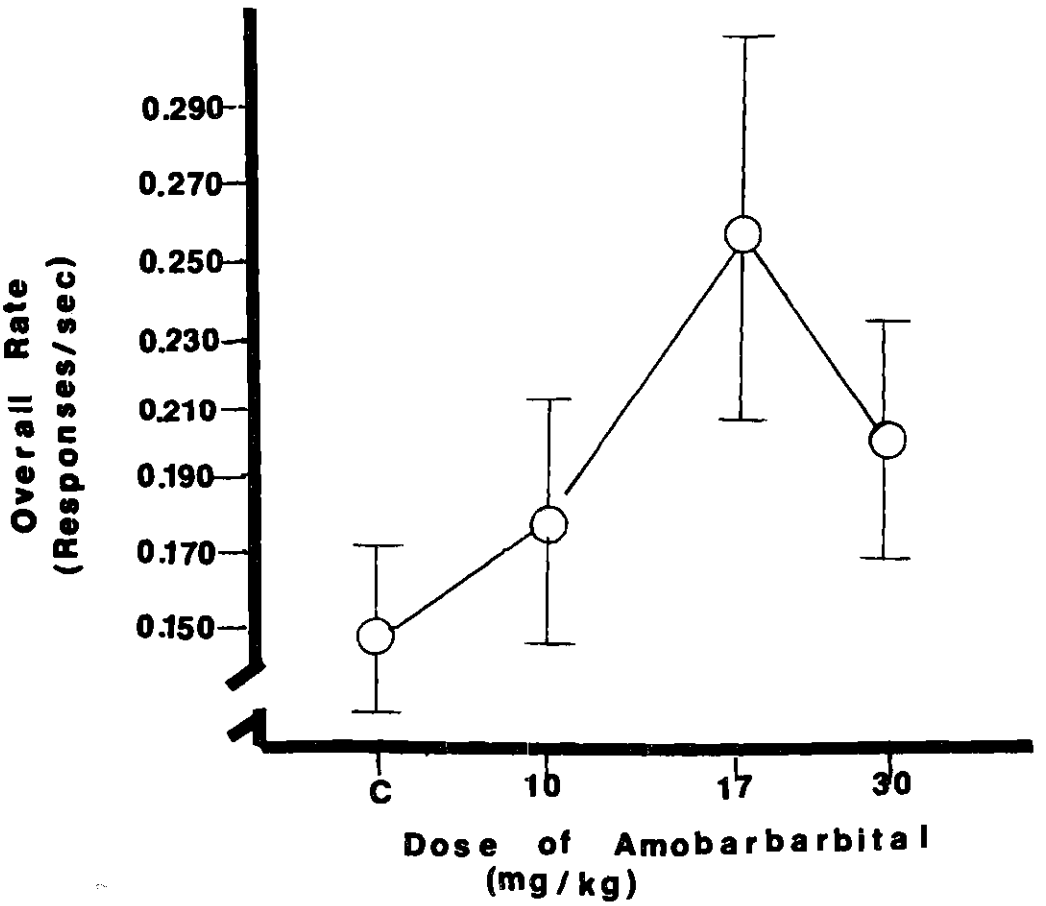

Figure 1. Dose Response Curve for Rats. (Overall rates of responding under the FI 10 min condition are plotted as a function of the mean control rate and mean drug rates at three dose levels of amobarbital. Each data point is the mean rate computed for five rats. Approximately three determinations at each dose level were made. Vertical lines signify ± standard error. The abscissa is a logarithmic scale.)

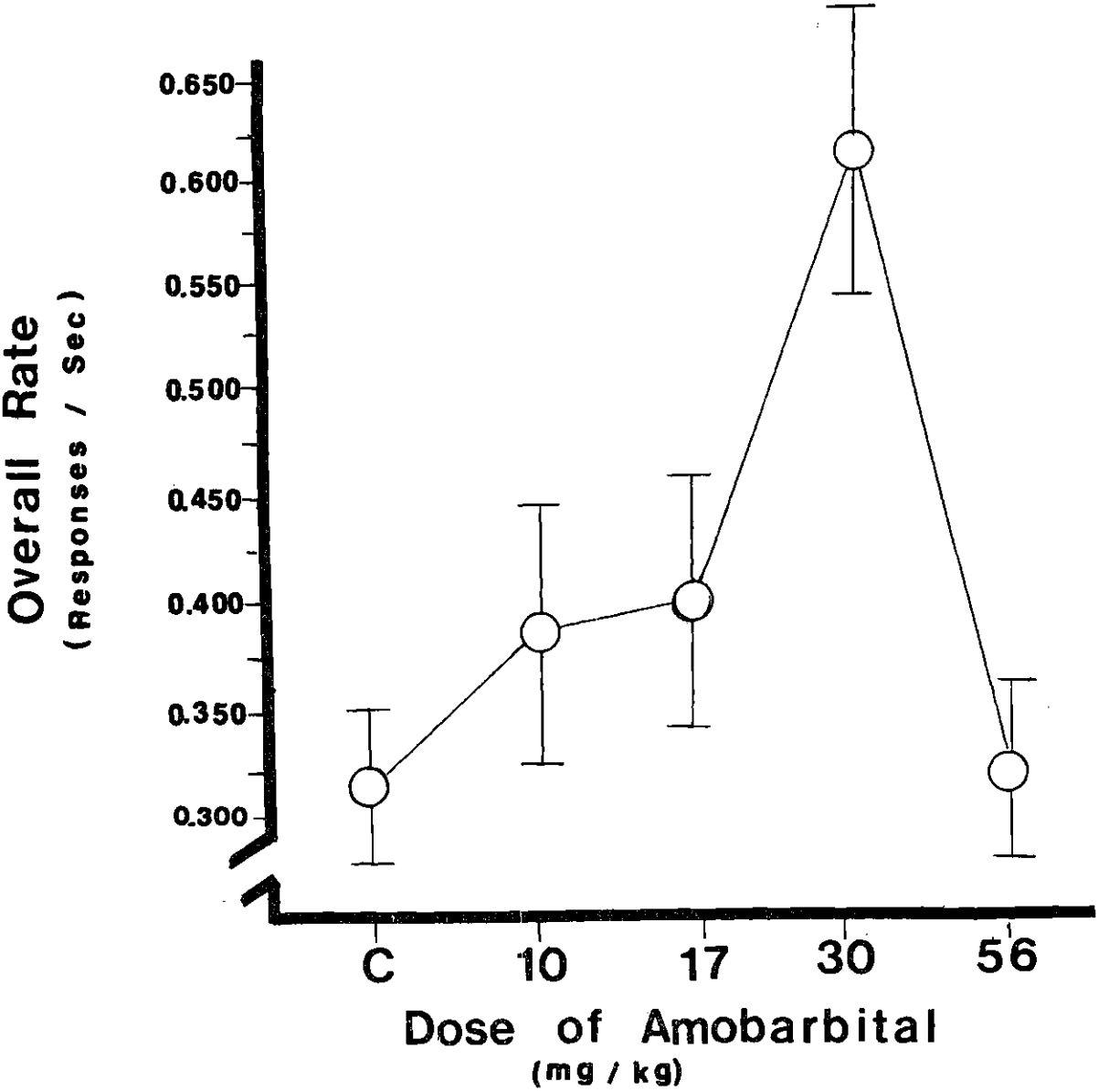

Figure 2. Dose Response Curve for Pigeons. (Overall rates of responding under the FI 10 min condition plotted as a function of the mean drug rates at three dose levels of amobarbital. Each data point is the mean rate computed for four pigeons. Two determinations were made at each dose level. Vertical lines signify ± standard error.)

for the pigeons were progressively increased at the 10, 17 and 30 mg/kg doses and decreased considerably at the 56 mg/kg dose.

For all subjects, the fixed-interval responding was characterized by the typical pattern of increasing rates of responding from very low rates of responding early in the interval to progressively higher rates toward the end of the interval. Quarter-life values were computed as a numerical index of the pattern of increasing rates of responding throughout the interval. The quarter-life is the percentage of the interval that has elapsed when the subject has emitted twenty-five percent of all responses that are emitted during the interval. A quarter-life value of at least fifty was typically exhibited by all rats and pigeons. This indicates that at least five minutes of the interval had elapsed when twenty-five percent of all responses made during the interval were emitted. Figures 3 and 4 show a plot of the quarter-life as a function of dosage for the rats and pigeons respectively. The quarter-life values decreased progressively as the dose level was increased indicating that as the dosage increased, less of the interval had elapsed when twenty-five percent of the responses were emitted. That is, rates of responding became higher early in the interval as the dosage increased.

Drug rate-dependency functions also reveal that

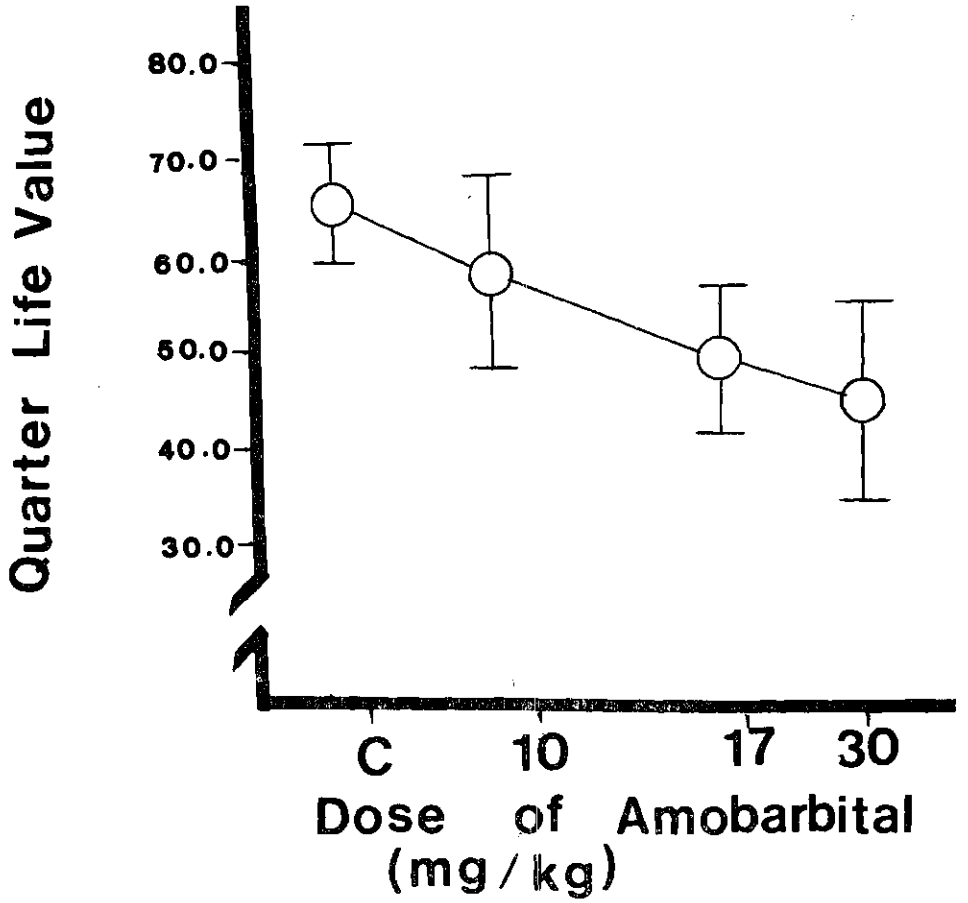

Figure 3. Dose Quarter Life Curve for Rats. (Quarter life values under the FI 10-min condition are plotted as a function of the mean control rate and mean drug rates at three dose levels of amobarbital. Each data point is the mean quarter life value for five rats. Three determinations were made at each dose level. Vertical lines signify ± standard error. The abscissa is a logarithmic scale.)

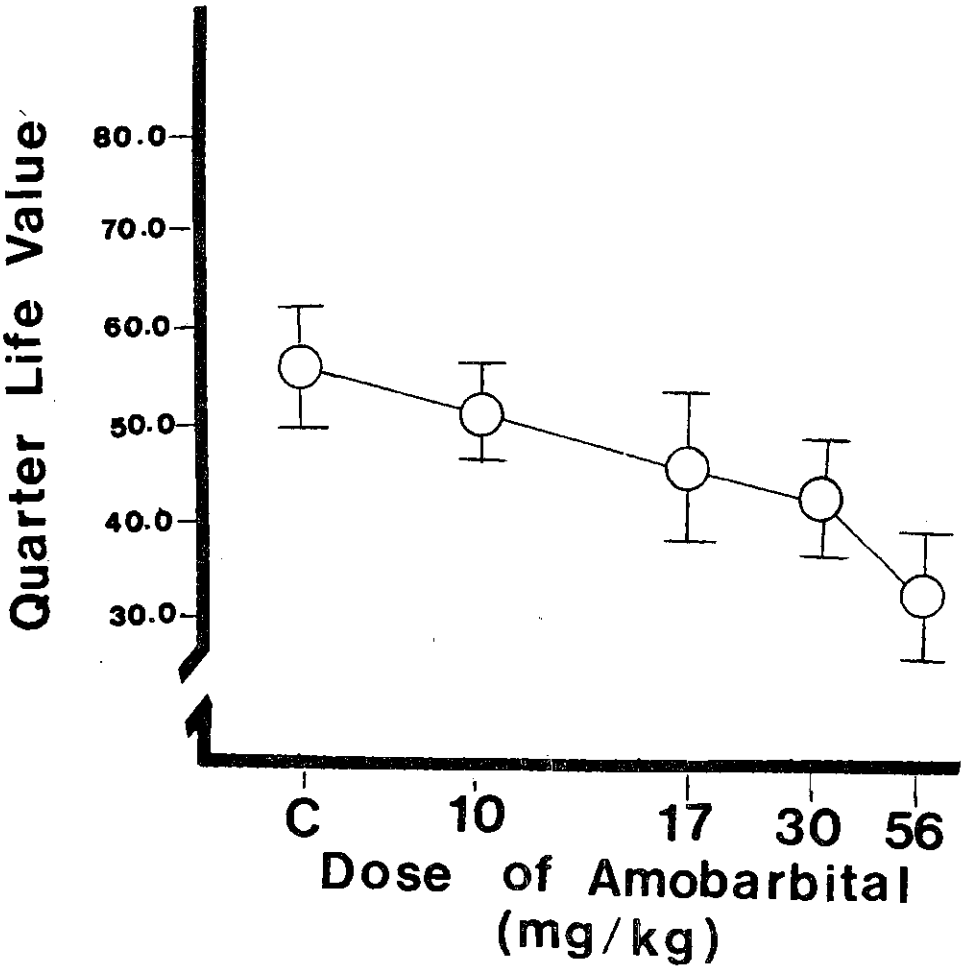

Figure 4. Dose Quarter Life Curve for Pigeons. (Quarter life values under the FI 10-min condition are plotted as a function of the mean control rate and mean drug rates at three dose levels of amobarbital. Each data point is the mean quarter life value for four pigeons. Two determinations were made at each dose. Vertical lines signify ± standard error. The abscissa is a logarithmic scale.

amobarbital greatly affects responding under the fixed-interval 10-min schedule. The rate-dependency functions describes the relationship between the drug rate of responding and the control rate of responding. Rates of responding were recorded for each 1-min segment of the ten-minute interval. The ratio of drug rate to control rate was computed for each 1-min segment for each dose level of amobarbital. This ratio indicates the proportionate increase (or decrease) in rate of responding that occurred under the drug in that 1-min segment. When these ratios were multiplied by 100 to remove decimals and plotted as a function of the control rates on a log-log scale, a linear function with negative slope resulted. Typical rate-dependency functions for two doses (10 and 30 mg/kg) are presented for Rat B-2 in Figure 5 and for Pigeon 276 in Figure 6. These rate-dependency functions demonstrate the typical inverse relationship that exists between drug rate of responding and control rate of responding when amobarbital is administered. That is, low control rates are increased and high control rates are decreased. If no change in rate occurs as a result of the administration of the drug, the ratio of drug rate to control rate would be one and since the ratios are multiplied by 100, all data points would fall on the 100 percent line indicating no change.

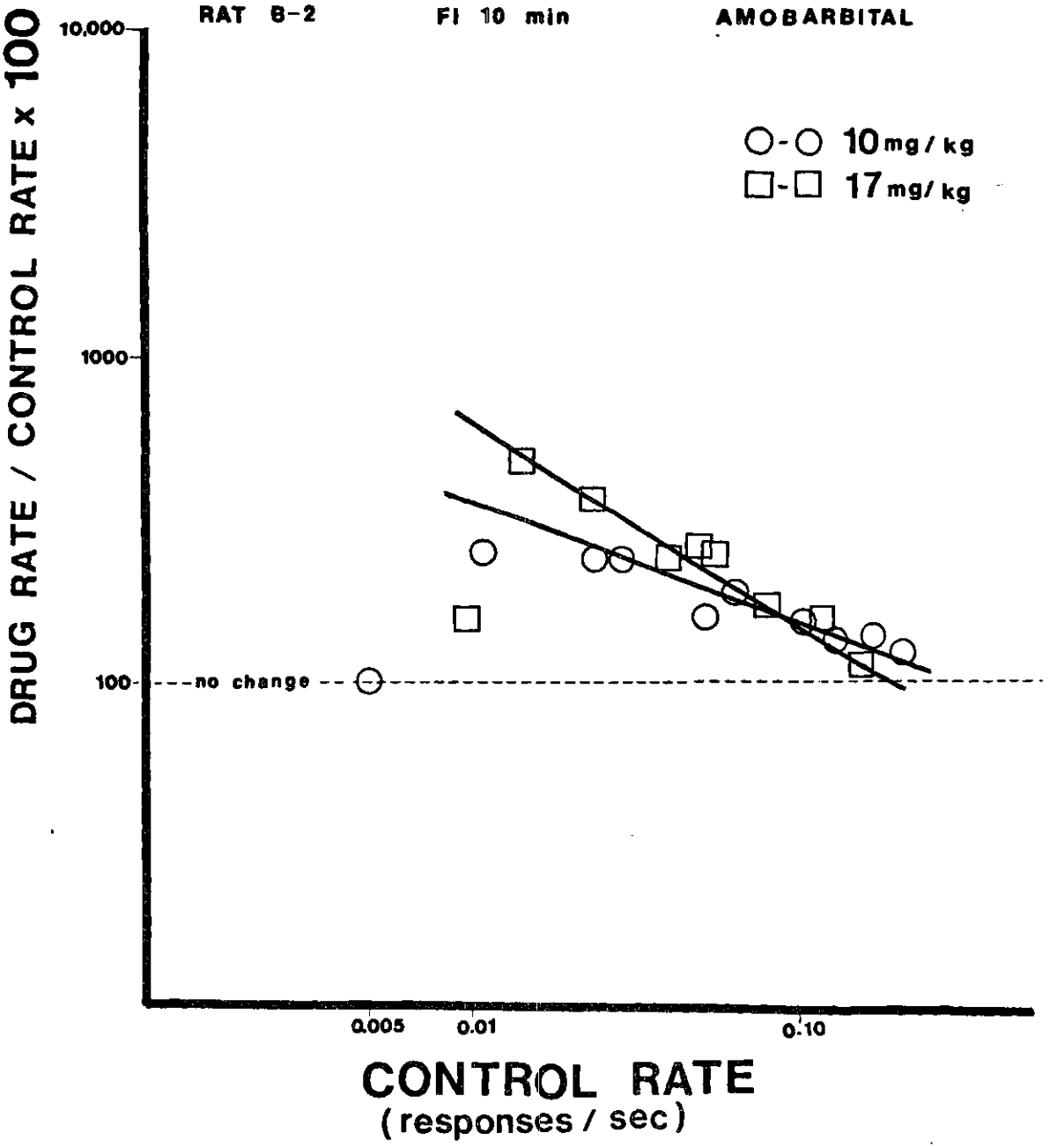

Figure 5. Rate-Dependency Functions for Rat B-2 Under an FI 10-Min Schedule. (Ordinate: rate after amobarbital expressed as percent of control. Abscissa: control rate during individual 1-min segments of the FI. Ordinate and abscissa are logarithmic.)

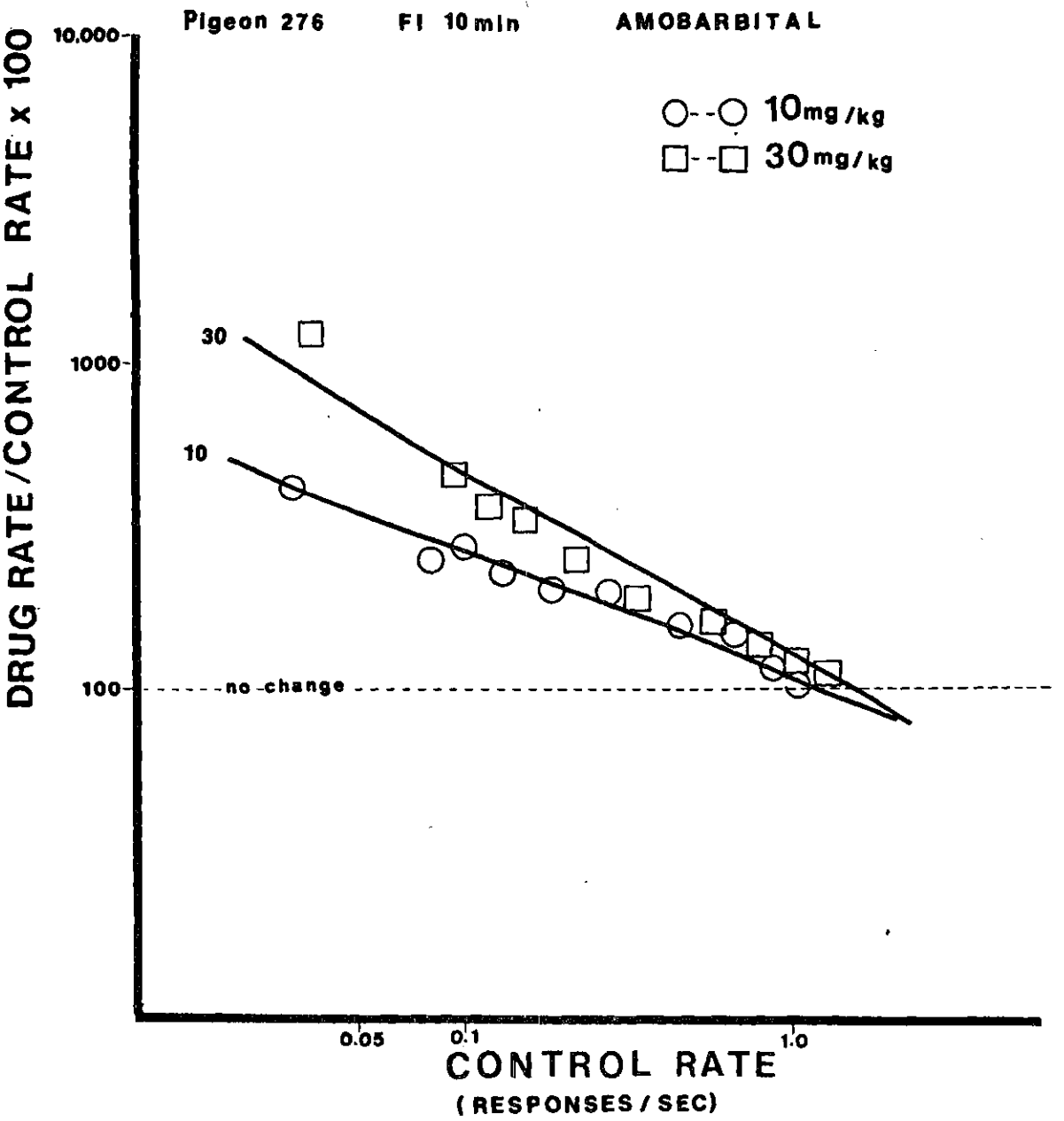

Figure 6. Rate-Dependency Functions for Pigeon 276 Under an FI 10-Min Schedule. (Ordinate: rate after amobarbital expressed as percent of control. Abscissa: control rate during individual 1-min segments of the FI. Ordinate and abscissa are logarithmic.)

Rate-dependency functions were demonstrated by all five rats at the 17 mg/kg dose of amobarbital and by four of the five rats at the 10 and 30 mg/kg dose. Rat B-8 demonstrated no change in rates at the 10 mg/kg dose and for Rat B-7 all rates were greatly depressed at the 30 mg/kg dose since this animal slept throughout most of the drug session.

Three of the four pigeons demonstrated rate-dependency functions at the 10 and 17 mg/kg dose. Pigeon 110 demonstrated no change in rate at these two doses. All four pigeons, however, demonstrated rate-dependency functions for the 30 mg/kg dose.

In general, the effect of increasing the dose of amobarbital was to raise the slope of the rate-dependency function. Cursory examination of the rate-dependency functions in Figures 5 and 6 indicate that the slope for the 30 mg/kg dose was generally much higher than the 10 mg/kg slope. Generally, there was little difference between the regression lines for the 17 and 30 mg/kg doses. The regression lines for the three doses tended to intersect at the higher control rates since the higher control rates were not raised very much by the administration of amobarbital at any of the dose levels and in a few cases they were slightly decreased. The intercept and slope for each regression line is presented in the Appendix in Table 1

for the rats and in Table 2 for the pigeons. The slope of each regression line was tested against the hypothesis that the true population slope was zero. This hypothesis was tested using a "t" test described by Goldstein (1964, p.146). As indicated in Tables 1 and 2, the slopes of most of the regression lines were significant at the 0.01 level for the pigeons and at the 0.05 level for the rats when compared with a line having a slope of zero (no effect). When comparisons were made between regression lines obtained at the different dose levels using a "t" test for the significance of a difference between two slopes (Goldstein, p.144), no differences were found.

FI 10-Min Plus S^{Δ} Schedule

Performance on the fixed-interval 10-min plus S^{Δ} schedule stabilized within forty sessions for the rats and within eighteen sessions for the pigeons. Rates of responding in the S^{Δ} segments (minutes 1,3,5,7 and 9) were much lower than the rates of responding in the S^{D} segments. These differences between S^{D} and S^{Δ} rates may be observed in Figure 7 for Rat B-2 and in Figure 8 for Pigeon 237F. These figures present the mean rates of responding for each one minute segment of the fixed-interval 10-min plus S^{Δ} schedule. The S^{Δ} rates were much lower than comparable rates under the simple fixed-interval schedule.

Drug rate-dependency effects were again demonstrated

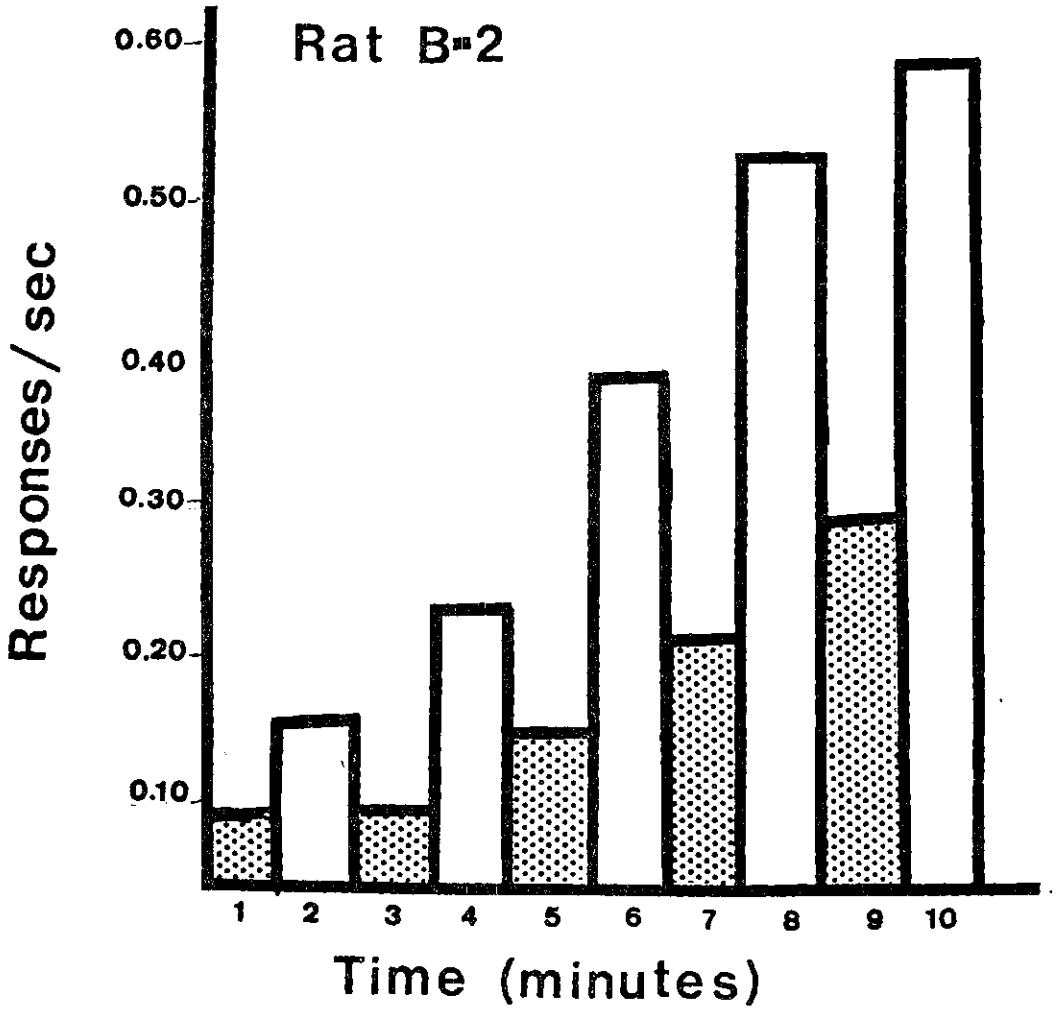

Figure 7. Rates of Responding in Each Individual One Minute Segment of the FI 10-min plus S^{Δ} Schedule for Rat B-2. (Open bars: mean rates of responding in S^{D} segments. Stippled bars: mean rates of responding in S^{Δ} segments.)

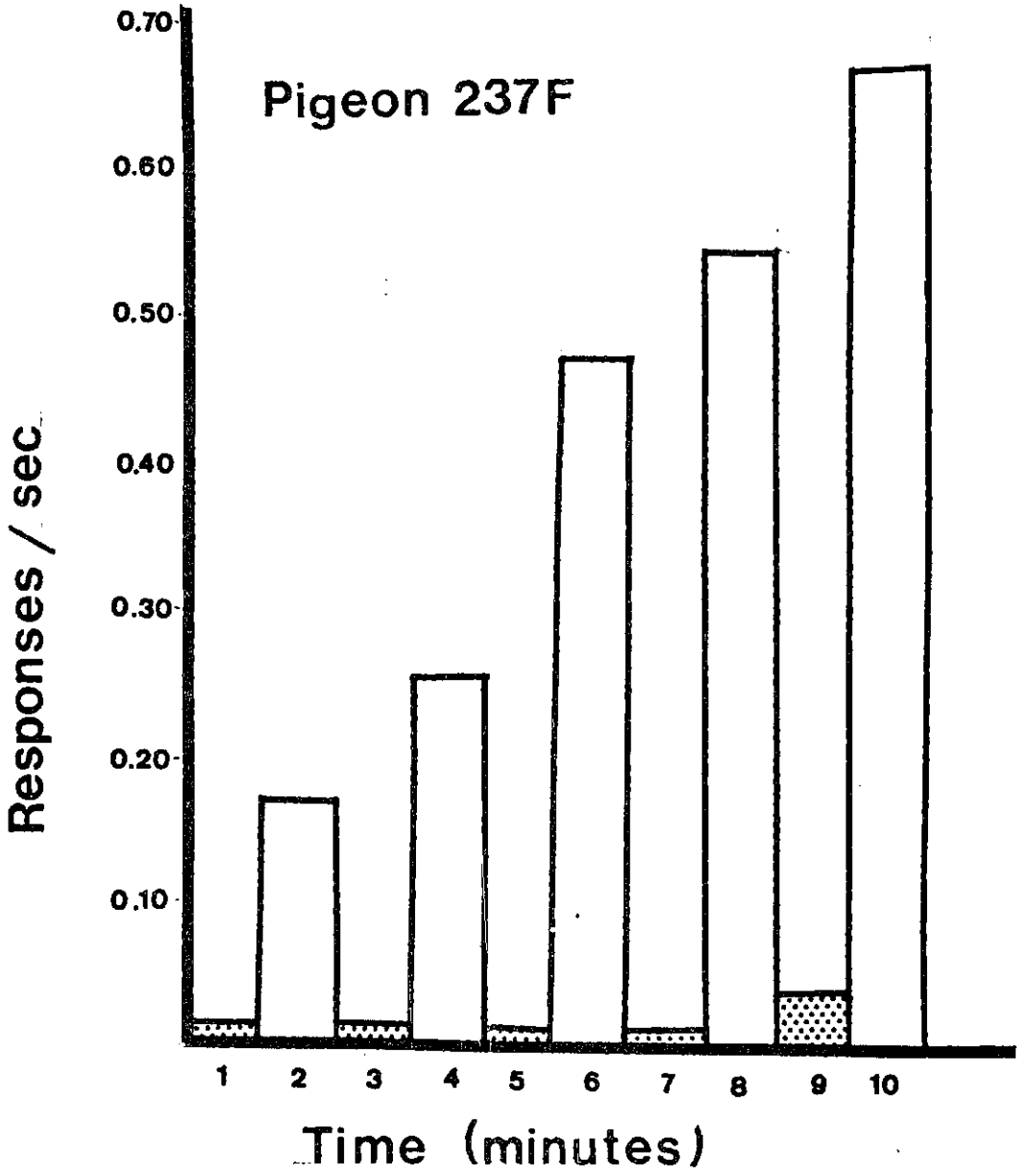

Figure 8. Rates of Responding in Each Individual One Minute Segment of the FI 10-min plus S^{Δ} Schedule for Pigeon 237F. (Open bars: mean rates of responding in S^{D} segments. Stippled bars: mean rates of responding in S^{Δ} segments.)

under the FI 10-min plus S^{Δ} condition when amobarbital was administered. However, rate-dependency functions for the rats could be demonstrated only at the 10 mg/kg dose level. The rate-dependency function for Rat B-2 is presented in Figure 9. As shown by Gollub (1971) the rates of responding during minutes one and two were not increased proportionately as much as the rates in the remaining eight one-minute segments. Consequently, these two data points were not included in the least squares analysis for the rats. Both the S^{Δ} and the S^{D} data points fell along the same regression line for all rats. There was little difference between the regression lines produced under the FI 10-min schedule versus the FI 10-min plus S^{Δ} schedule at the same dose level.

Rate-dependency was demonstrated at 17 and 30 mg/kg doses for three of the four pigeons. Only one of the pigeons, Pigeon 354, demonstrated rate-dependency at the 10 mg/kg dose. Figure 10 presents rate-dependency functions for Pigeon 276 at the 17 mg/kg dose. S^{Δ} and S^{D} points fell along the same line for all pigeons at both the 17 and 30 mg/kg doses. As was found with the rats, there was little difference between the rate-dependency functions produced under the FI 10-min and those produced by the FI 10-min plus S^{Δ} condition.

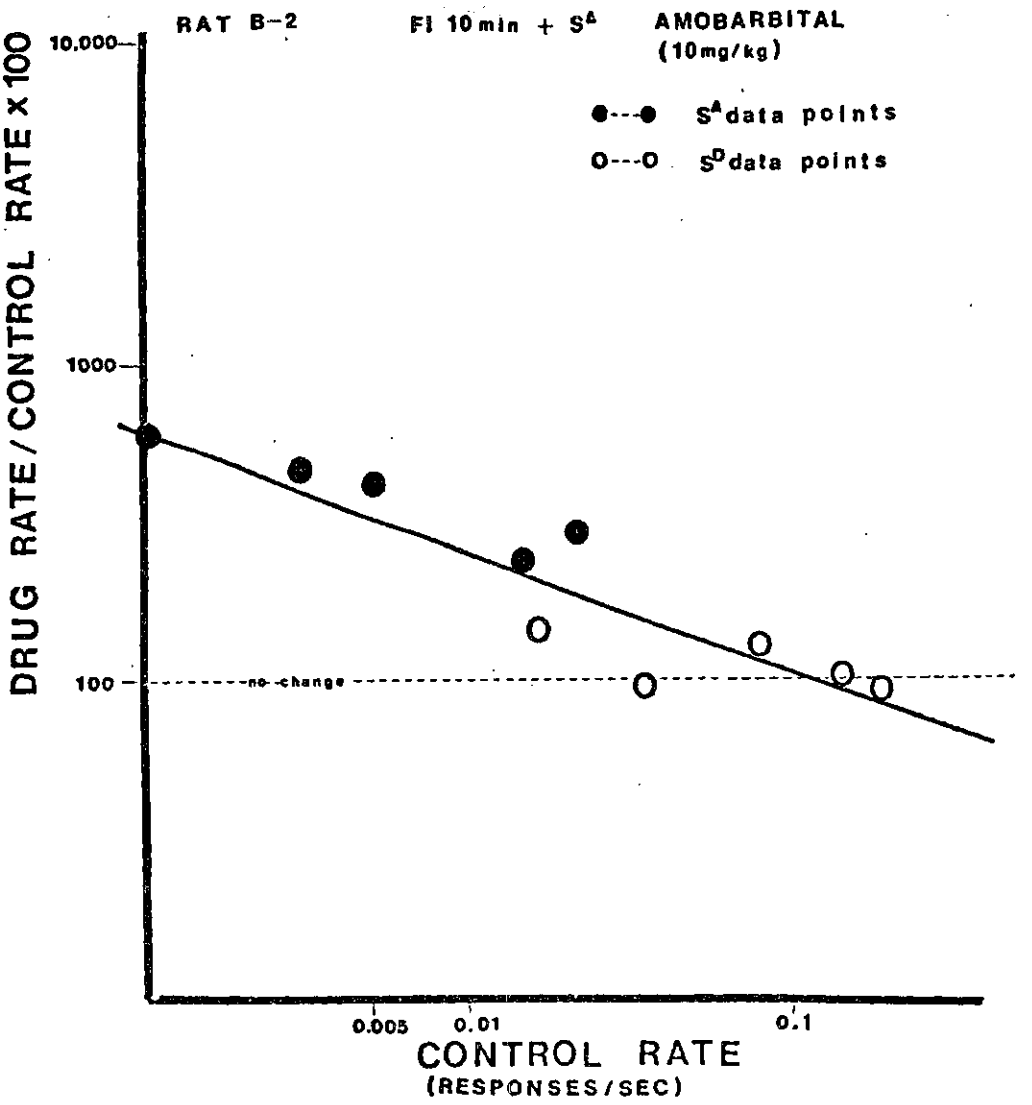

Figure 9. Rate-Dependency Function for Rat B-2 Under the FI 10-Min Plus S^{Δ} Schedule. (Ordinate: rate after amobarbital expressed as percent of control. Abscissa: control rate during individual 1-min segments of the FI. Ordinate and abscissa are logarithmic. Open circles: S^{D}. Closed circles: S^{Δ}. Each point represents mean of three determinations. Both S^{D} and S^{Δ} points fell along the same regression line.)

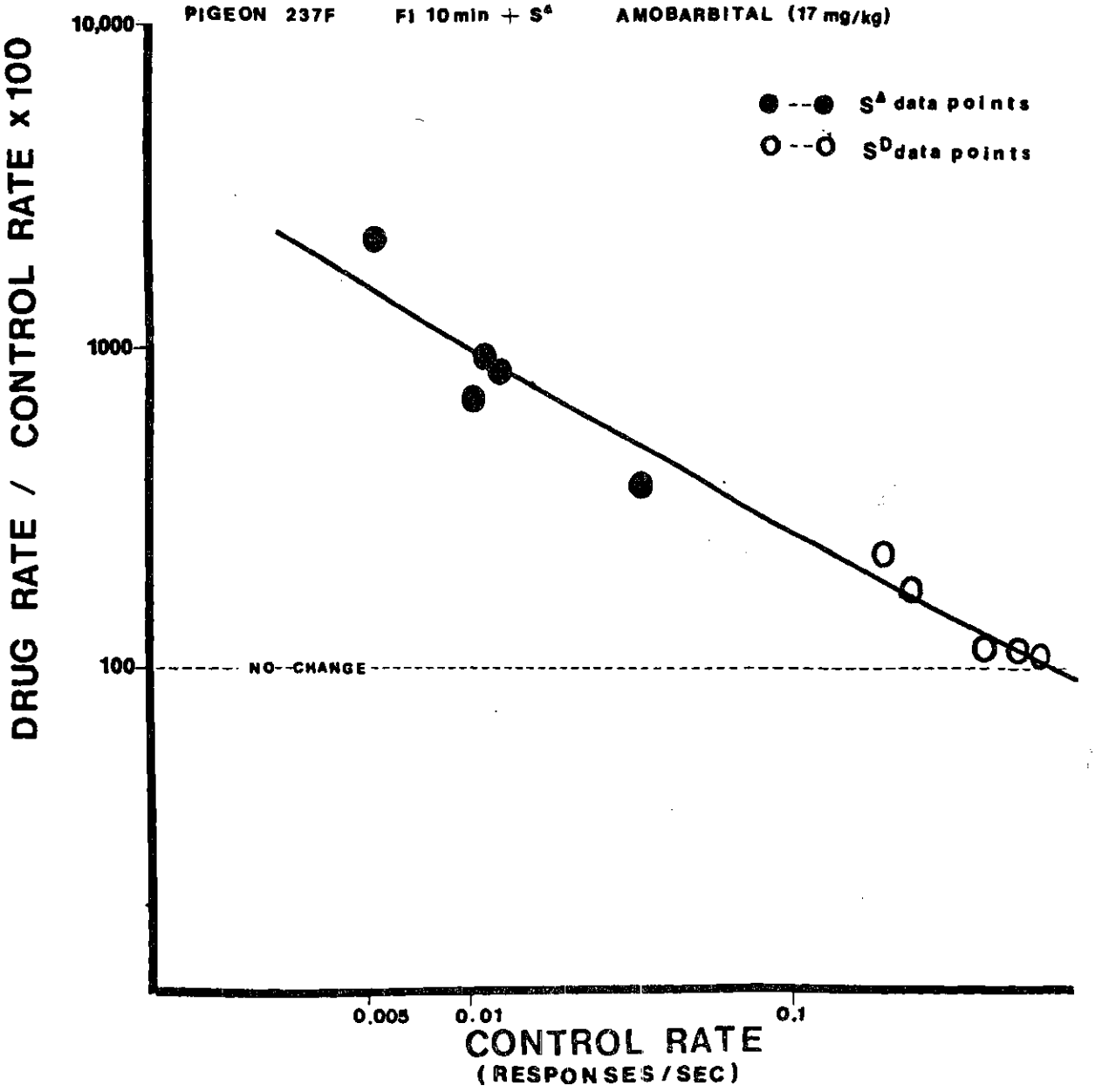

Figure 10. Rate-Dependency Function for Pigeon 237F Under the FI 10-Min Plus S^{Δ} Schedule. (Ordinate: rate after amobarbital expressed as percent of control. Abscissa: control rate during individual 1-min segments of the FI. Ordinate and abscissa are logarithmic. Open circles: S^{D}. Closed circles: S^{Δ}. Each point represents mean of three determinations. Both S^{D} and S^{Δ} points fell along the same regression line.)

FI 10-Min Plus S^{Δ} Plus Shock. (Rats Only)

When a brief electric shock was added to the S^{Δ} condition, at least seven sessions were run at each intensity (0.13, 0.25, 0.50 and 0.80 ma) before amobarbital was administered to allow the baseline to stabilize. However, there were no detectible differences in baseline performance as a result of the addition of the electric shock. Two doses of amobarbital were used, 10 and 17 mg/kg. However, only the results of the 10 mg/kg dose will be discussed since the rats slept throughout most of the daily sessions when the 17 mg/kg dose was administered.

No rate-dependency effect was demonstrated by Rat B-2 at any shock level. Rate dependency functions were demonstrated at all shock intensities by Rats B-3 and B-8. For Rats B-6 and B-7, rate dependency functions were demonstrated at the 0.13 and 0.25 ma levels but not at the 0,50 and 0.80 ma levels. Thus, the general trend seems to be that rate dependency functions are obtained at low intensities of shock with four of the five rats demonstrating rate-dependency at the two lower shock levels. The rate-dependency function for Rat B-8 at the 0.25 ma level is presented in Figure 11. At high shock levels (0.50 and 0.80 ma) however, only two of the five rats demonstrated rate-dependency functions. The other three rats showed no

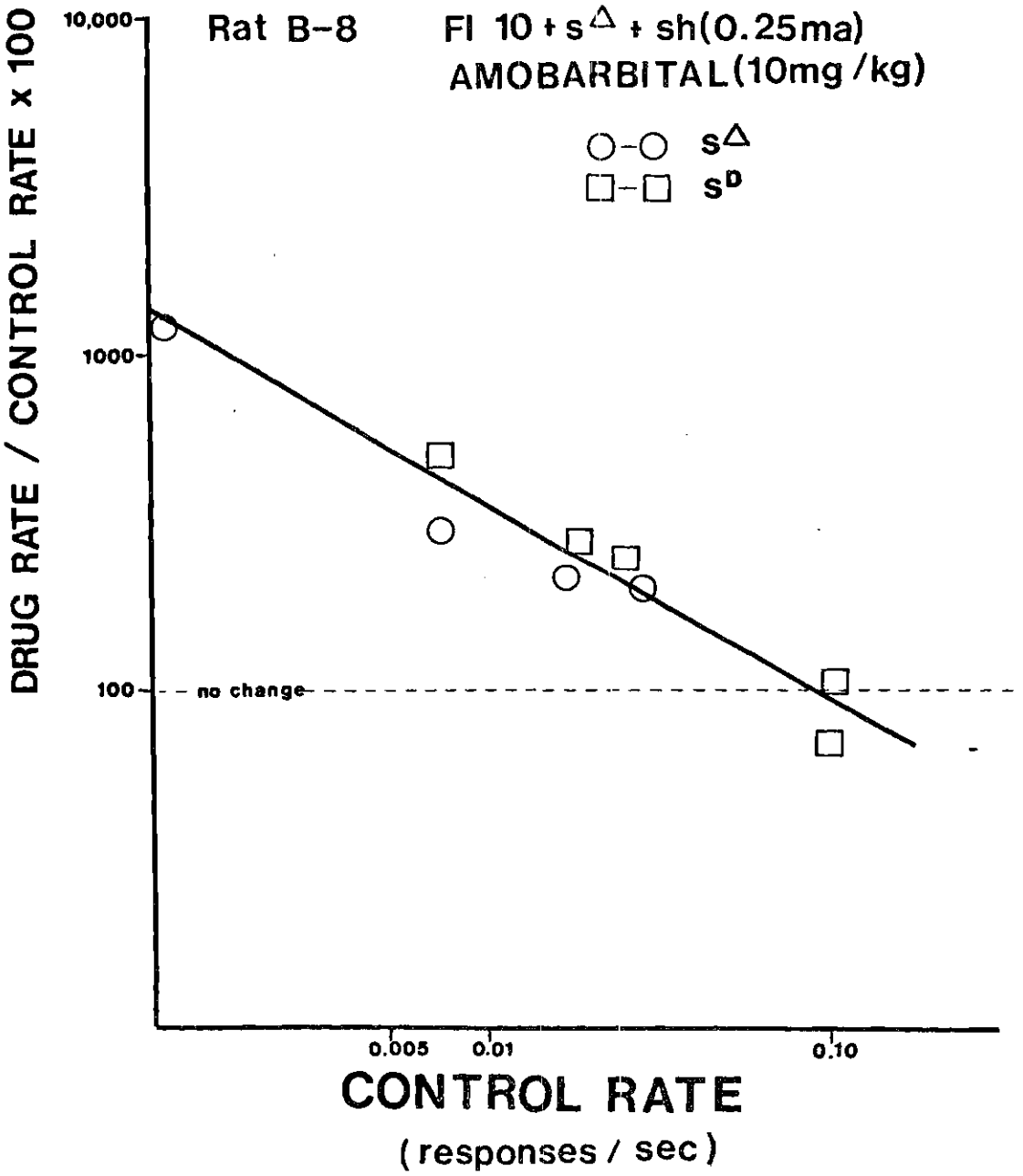

Figure 11. Rate-Dependency Function for Rat B-8 Under an FI 10-Min Plus S^{Δ} Plus Shock (0.25ma) Schedule. (Ordinate: rate after amobarbital expressed as percent of control. Abscissa: control rate during individual 1-min segments of the FI. Ordinate and abscissa are logarithmic. Open circles: S^{D}. Closed circles: S^{Δ}. Each point represents mean of two determinations. Both S^{D} and S^{Δ} points fell along the same regression line.)

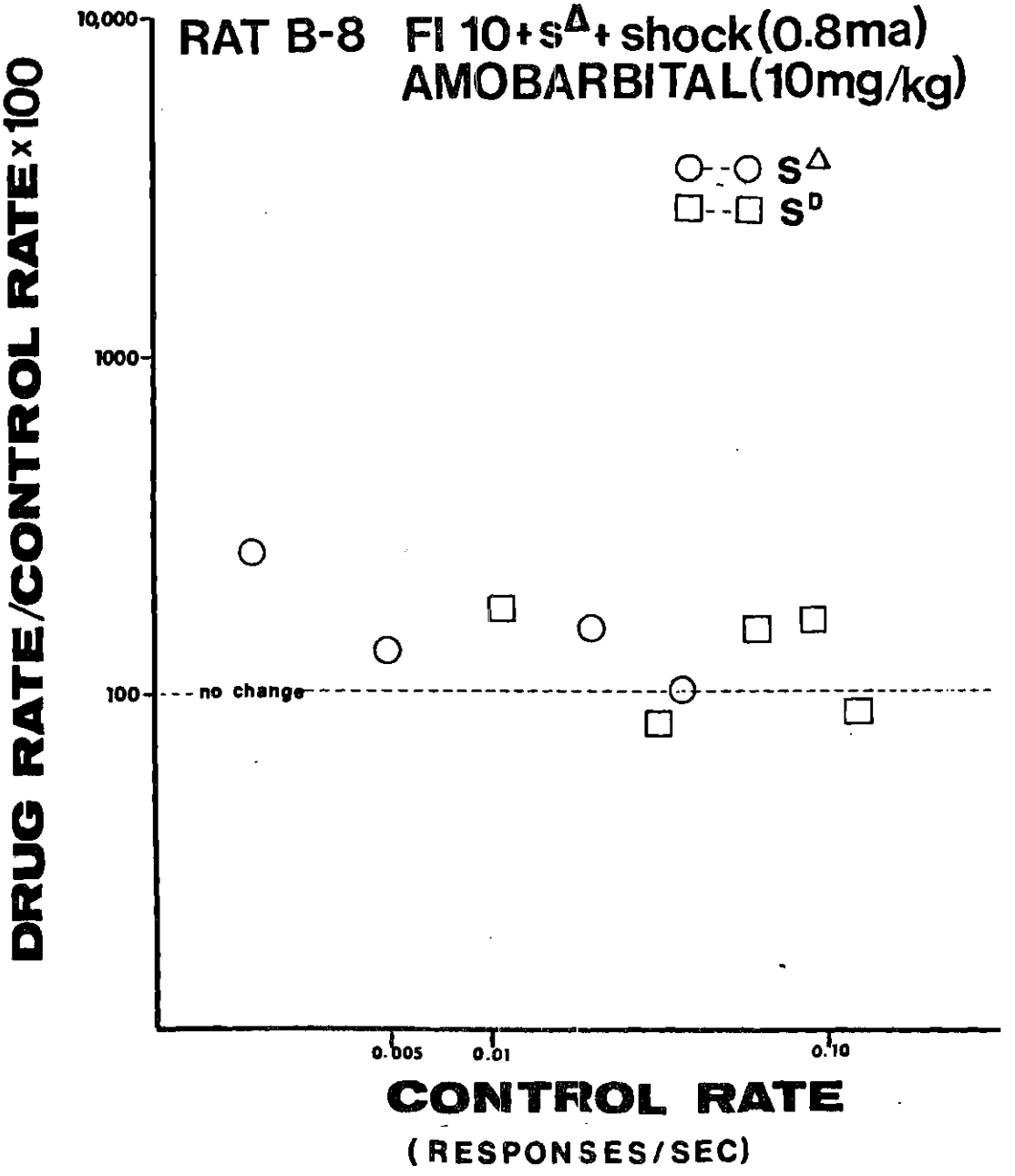

Figure 12. Lack of Rate-Dependency for Rat B-8 Under an FI 10-Min Plus S^{Δ} Plus Shock (0.80ma) Schedule.

change in rate as a result of the administration of amobarbital. Figure 12 presents the performance of Rat B-8 at the 0.80 ma shock level. All data points fell along the 100 percent line indicating that there was little change in response rates as a result of the administration of amobarbital. Thus the rate-dependency effect was abolished at high shock levels for three rats, but for the two rats that demonstrated rate-dependency, the high control rates were considerably decreased under the drug amobarbital. For all the rate-dependency functions obtained under this condition, both the S^D and S^Δ data points fell along the same regression line.

FI 10-Min Plus S^Δ Plus S^P. (Pigeons Only)

The pigeons were run 14 sessions under the S^Δ condition with the brief stimulus paired with food to allow for any stabilization of the baseline that was necessary. There were, however, no detectible differences in baseline performance as a result of the added S^P. Amobarbital was then administered.

Rate-dependency functions were obtained by two birds, Pigeons 237F and 276 at all dose levels. Pigeon 354 demonstrated rate-dependency only at the 30 mg/kg dose and Pigeon 110 did not show any changes in rate at any of the three dose levels.

The rate-dependency function for Pigeon 237F is

presented in Figure 13. As was the case for all the rate-dependency functions obtained under this condition, both the S^D and S^Δ data points fell along the same regression line. There were no differences between the regression lines obtained under the FI 10-min plus S^Δ plus S^P and either the simple FI 10-min or the FI 10-min plus S^Δ condition. For two regression lines obtained for Pigeon 354, the S^D and S^Δ data points could be best fitted by two, rather than one, regression lines. Neither of these lines were significant when tested against the hypothesis of zero slope. Cursory examination of the graph of this data further suggested that no real effect was demonstrated.

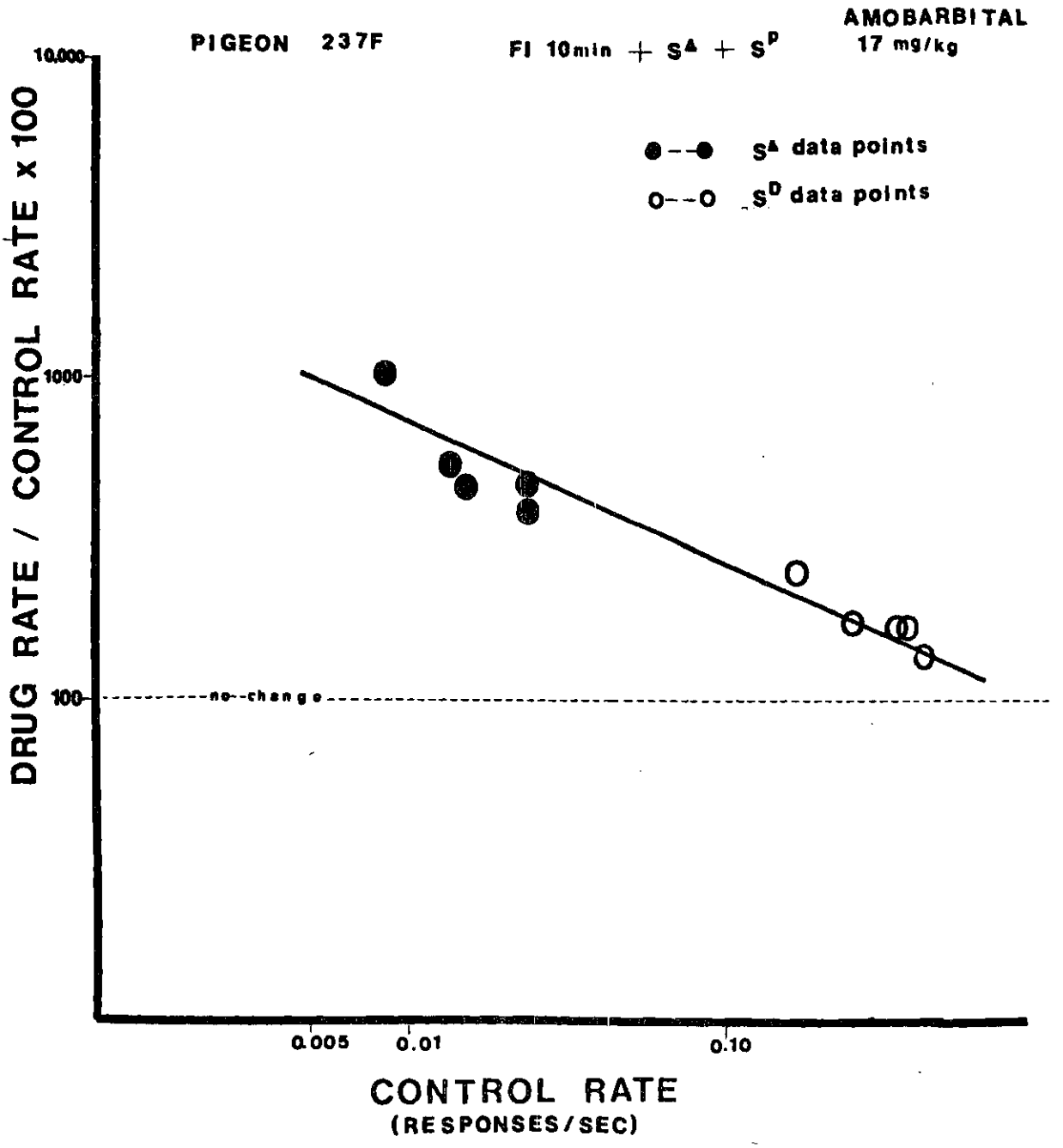

Figure 13. Rate-Dependency Function for Pigeon 237F Under an FI 10-Min Plus S^{Δ} Plus S^{D} Schedule. (Ordinate: rate after amobarbital expressed as percent of control. Abscissa: control rate during individual 1-min segments of the FI. Ordinate and abscissa are logarithmic. Open circles: S^{D}. Closed circles: S^{Δ}. Each point represents mean of six determinations. Both S^{D} and S^{Δ} points fell along the same regression line.)

CHAPTER IV

DISCUSSION

The effects of drugs on behavior may be understood, in part, on the basis of two factors: (1) the probability (rate) of responding, and (2) the prevailing stimulus conditions. Often the effects of drugs on control rates are to increase low control rates and to decrease high control rates. This inverse relationship between drug rates and control rates is an expression of a drug rate-dependency effect.

In the present experiment, the changes in rates of responding effected by amobarbital were found to be inversely related to control rates of responding under several conditions. Such a rate-dependency effect was demonstrated by all pigeons under both a simple fixed-interval 10-min schedule and under a fixed-interval 10-min schedule with superimposed S^{Δ}s. These results are consistent with those of Dews (1964) and McKearney (1970) who also studied the performance of pigeons under a simple schedule.

Similar results, however, have not previously been demonstrated using rats as subjects. While the rats also showed rate-dependency effects under the simple fixed-interval 10-min schedule, their performance under the S^{Δ} schedule was more influenced by the particular dosage used.

Three dose levels (10, 17 and 30 mg/kg) of amobarbital were studied under both schedules for both rats and pigeons. At least some of the rats and pigeons demonstrated a rate-dependency effect at every dose level under the simple fixed-interval procedure. When the S^{Δ}s were added, however, performance of the rats under the higher dose levels was considerably influenced. Whereas the pigeons again demonstrated rate-dependency at all three dose levels, the rats showed rate-dependency effects only at the 10 mg/kg dose. At the 17 mg/kg dose the rats slept throughout the greater portion of the daily session and at the 30 mg/kg dose level, they slept throughout the entire session without making even one response. Thus in the presence of the S^{Δ} stimulus, the effectiveness of the drug in terms of inducing sleep in the animal was minimally affected at the higher dose levels. Since the presence of the S^{Δ} stimuli reduces the rat's activity with respect to the operant response, it may make the animal more conducive to sleeping. However, why this should occur with the rats and not with the pigeons is not apparent at this time.

When a particular behavior is under the control of strong environmental stimuli, the effects of the drug on rates of responding may be minimized. McKearney (1970) found, for instance, that the brighter the houselight (S^{Δ}), the less response rates were increased under amobarbital.

In conditional discriminations, Holz (1971) found that error rates of responding were increased less than correct rates of responding when chlorpromazine was administered.

Such "stimulus-dependent" effects suggest the possibility of using drugs as tools to study the extent of control that a particular stimulus exerts on behavior. Both Laties and Weiss (1966) and McKearney (1970) suggested that rate-dependency may be modified or eliminated when responding is under the control of strong environmental stimuli. A more functional approach might be to reason that the strength of stimulus control may be inferred by the extent to which rate-dependency functions are modified.

The question of strength of stimulus control becomes especially challenging when various stimulus conditions control a zero or near zero rate of responding. Such stimuli are often termed "inhibitory". There are two basic ways of studying the inhibitory properties exhibited by a particular stimulus (Hearst, et al., 1970). One is to look at dimensional control; i.e., the effect on responding produced by varying some stimulus dimension. That is, a stimulus is said to have inhibitory properties if a U-shaped generalization gradient with a minimum at S- is obtained when the particular stimulus is varied along one of its physical dimensions. This method of studying stimulus control has been referred to as a stimulus

dimensional effect.

The second way of studying inhibitory stimulus control is to determine if a particular stimulus develops, during conditioning, the capacity to decrease response strength below the level occurring when that stimulus is absent. However, although demonstration of a response decrement is a necessary condition for establishing inhibition, it is not a sufficient condition. Such a stimulus must also be shown to be inhibitory by some independent test. Otherwise, the response decrement may occur simply because the stimulus is neutral and consequently has no relevance for the organism, or it may be an excitatory stimulus which, as a result of conditioning, becomes less excitatory. If the latter is the case, then having the one concept of excitation would be more parsimonious than including the second concept of inhibition.

Many of the methods for studying the inhibitory properties of a stimulus have attempted to produce a high enough output of behavior so that inhibitory effects (decrements in responding) could be distinguished from no effect at all. However, many stimuli which may be inhibitory and many stimuli which may be neutral both often command zero level of responding. There are very few procedures for dealing with this problem, and perhaps the study of how drugs interact with prevailing stimulus conditions may

elucidate such investigations.

All of the present experiments involved stimulus conditions which controlled near-zero levels of responding, yet drug effects differed in relation to these procedures. The third experimental condition for the rats involved terminating the superimposed S^{Δ} periods with the presentation of a brief electric shock, a situation similar to the conditioned suppression procedure of Estes and Skinner (1941). It was found that at the low levels of shock (0.13 and 0.25 ma), rate-dependency functions are obtained, while at the higher levels of shock (0.50 and 0.80 ma), rate-dependency is abolished. Such a modification of the rate-dependency function suggests that the presentation of electric shock at increasing amperage levels commands an increasing degree of stimulus control over the organism's operant responding. Thus, under the present schedule conditions, as the shock level increased, the probability increased that shock would be a more important determinant of the behavioral effects of amobarbital than was the control rate of responding. Stein, Brady and Ray (1958), as well as Verhave (1955), have found that the intensity of electric shock is one factor that determines the degree of suppression that will be obtained in the conditioned suppression procedure. Thus the intensity of the shock may be one factor which has contributed to the diverse drug effects which have been

found using this procedure.

An additional finding of the current study was that the use of electric shock seems to influence the the total stimulus environment and total pattern of responding of the organism rather than being limited to only those stimuli with which the presentation of the shock is paired. There was no change in rate as a result of the administration of amobarbital in either the S^{Δ} or the S^{D} components. Thus the effect of using strong electric shock not only influenced the drug rate of responding in the S^{Δ} components, but the S^{D} components were also influenced. However, since in the absence of shock, the S^{Δ} rates were normally increased proportionally more than S^{D} rates under amobarbital, the effect of shock was proportionally greater for the S^{Δ} data points.

In the pigeon experiment, the third experimental condition consisted of terminating each S^{Δ} with the brief presentation of a stimulus which is paired with food, S^{P}. The procedure of pairing a stimulus with food has been shown to establish a stimulus as a conditioned reinforcer (cf. Marr, 1969). In this respect, this procedure is similar to positive conditioned suppression. Positive conditioned suppression, however, has previously been established only by using a primary reinforcer. Rate-dependency effects were demonstrated at all three dose levels under this

procedure and there was no difference between these rate-dependency functions and either those obtained under the simple fixed-interval or the fixed-interval with superimposed S^{Δ}'s. This suggests that the addition of the S^{P} did not appreciably affect the degree of stimulus control which the S^{Δ} commanded.

In turn, the results of these experiments indicate that there was no difference in the amount of stimulus control exerted by the S^{Δ} or the S^{Δ} plus S^{P} stimuli for the pigeons. However, in the rat experiment the amount of stimulus control exerted by the S^{Δ} plus shock was much greater than that held by the simple S^{Δ}, especially when high amperage levels were used. Thus, amobarbital was useful as a tool for detecting differences in the degree of stimulus control exerted by three stimulus procedures which produced very similar baseline performances.

One should not be left with the impression that drug effects can be totally understood in relation to the tendency of behavior to occur or the prevailing stimulus conditions. Such variables as schedule, motivation, physiological state, tolerance, individual history and many others (cf. Harvey, 1971) can also be of major importance. However, no behavioral situation of nontrivial complexity is likely to be devoid of rate-dependency or stimulus control considerations, rendering neglect of these variables perilous.

APPENDIX

Table 1. Regression Equations for the Rate-Dependency Functions for the Rats. (Data are slopes and intercepts of the regression analysis: log drug rate/control rate X 100 on log control rate. Rates are measured in responses per minute)

FI 10 min	Rat B-2	Rat B-3	Rat B-6	Rat B-7	Rat B-8
10 mg/kg	-.14* 2.29	-.48* 2.74	-.05 2.23	-.25* 2.34	-.06* 2.10
17 mg/kg	-.44* 2.70	-.47* 2.77	-.02* 2.00	-.67* 2.41	-.70* 2.61
30 mg/kg	.33 2.55	-.81* 3.08	-.31* 2.40	-.90 2.68	-.64 2.51
FI 10 min + S^{Δ}					
10 mg/kg	-.15* 2.54	-.25* 2.85	-.56* 2.02	-.32* 2.34	-.12* 2.27
FI 10 min + S^{Δ} + Shock					
(0.13 ma) 10 mg/kg	3.92 2.88	-.21* 1.98	-.76* 2.93	-2.41* 3.46	-3.48* 2.07
(0.25 ma) 10 mg/kg	.76 1.85	2.33* 3.48	-.36* 3.32	-.70* 2.58	-.56* 2.57
(0.50 ma) 10 mg/kg	-.55 2.07	-1.64* 3.06	-.25 2.08	-.79 2.59	2.70 2.95
(0.80 ma) 10 mg/kg	.18 2.10	1.45 2.98	-.22 1.28	-.14 2.19	-.71 2.51

* Slopes significantly different from zero, $p \leq .05$.

Table 2. Regression Equations for the Rate-Dependency Functions for the Pigeons. (Data are slopes and intercepts of the regression analysis: log drug rate/control rate X 100 on log control rate. Rates are measured in responses per minute.)

	P 354		P 237F		P 110		P 276	
FI 10 min								
10 mg/kg	-.35*	1.98	-.41*	1.90	-.34	2.10	-.35*	2.09
17 mg/kg	-.23*	2.05	-.78*	1.74	-.09	2.07	-.52*	2.04
30 mg/kg	-.45*	1.99	-.97*	1.62	.45	2.51	-.68*	1.92
FI 10 min + S^{Δ}								
10 mg/kg	-.48*	2.06	.91	2.86	.16	2.34	.01	1.87
17 mg/kg	.23	2.34	-.33*	1.97	-.28*	2.35	-.36*	2.06
30 mg/kg	-1.21*	1.52	-.41*	2.19	-1.39*	1.10	-.49*	1.92
FI 10 min + S^{Δ} + S^{P}								
10 mg/kg	-.12*	1.68	-.52*	1.94	.08	2.17	-1.26*	2.44
17 mg/kg	.36	2.43	-.40*	2.02	-.51	1.80	-.43*	2.17
30 mg/kg	.67	2.59	-.29*	2.25	-.45	1.80	-.32*	2.17

* Slopes significantly different from zero, $p<.05$.

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